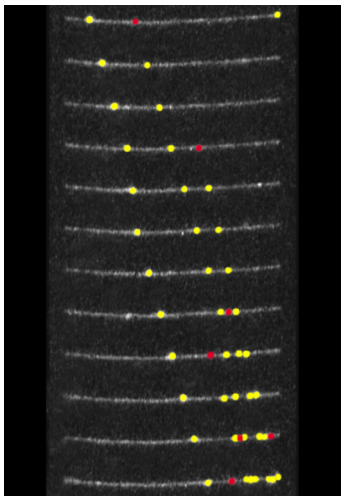
In This Issue



New kinesin (red) prefers to bind on the plus-end side of earlier kinesins (yellow).

Cooperative kinesin

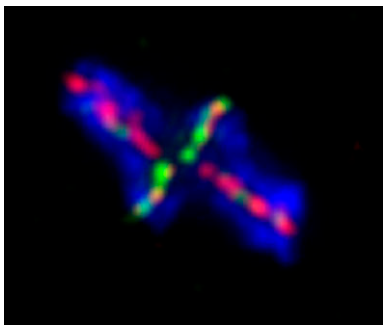
Train travel might be more efficient if the tracks helped the train along. On page 691, Muto et al. show that, unlike trains, kinesin motors do get a boost from their tracks—in this case, microtubules.

Muto and colleagues show that the binding of the plus end–directed motor kinesin to microtubules is cooperative. Like proverbial sheep, once one bead (or motor) bound to a filament, others followed suit in the same neighborhood. Cooperativity extended for several microns in either direction from the initial binding site, although newcomers were more than twice as likely to bind on the plus-end side of the earlier motors.

The findings suggest that microtubules are altered by kinesin in such a way that they attract more motors. ATP hydrolysis by kinesin was required for cooperativity, but how the energy is used is not known. The group is currently investigating how kinesin binding affects the movement of positive ions that surround the negatively charged microtubules. These changes may in turn alter kinesin motility.

The preference of kinesin for already-bound microtubules in vivo may establish a set of microtubules that is dedicated to vesicle trafficking. This idea fits well with previous findings that axonal microtubules carry either many vesicles or very few. JCB

Crossovers break SC symmetry



After recombination, SC proteins (green) remain only on the short chromosome axis.

At the start of meiotic prophase I, homologous chromosomes become aligned lengthwise. After recombination, chromosomes reconfigure to reduce contacts between homologues and prepare for bipolar spindle attachment. On page 683, Nabeshima et al. illustrate these rearrangements during worm meiosis and provide evidence that crossovers are symmetry-breaking events that promote the ungluing of lengthwise contacts between homologues.

During homologous recombination, proteins of the synaptonemal complex (SC) link aligned homologues. Later, the SC disassembles, leaving exchanged DNA and sister chromatid cohesion to link homologues.

The new images reveal that this SC disassembly is asymmetric. Crossovers usually occur at an off-center position, leaving a short and a long axis emerging from the spot of the crossover. SC components departed from the long axis first, but lingered on the short axis.

The crossover, or a precursor structure, seems to cue the unequal SC disassembly. Recombination mutants underwent more symmetric SC disassembly, but asymmetry was restored when crossovers were initiated by radiation-induced DNA breaks. The authors imagine that SC disassembly increases with distance from a crossover. As SC proteins bind cooperatively, loss of a few from the long end may start a chain reaction that clears that axis of the SC.

SC proteins lingered at the same spots where sister chromatid cohesion must be released in anaphase I. This partial cohesion release allows homologues to separate even as sister chromatids are still held together on the long axis. The lingering SC proteins may direct local release by recruiting the aurora kinase AIR-2, which concentrates on the short axis at the end of prophase. JCB

Myristoylation versus SRP

The machineries for myristoylation and cotranslational translocation fight over a substrate, as shown by Colombo et al. on page 735. The competition results in dual locales for the protein caught in the middle, called b5R.

b5R is a flavoprotein with two homes: one in the ER membrane, where it functions in lipid metabolism, and another in the mitochondrial outer membrane (MOM), where it regenerates reduced ascorbate. b5R is myristoylated in both locations. But the modification is only required for the mitochondrial targeting, as mutation of the myristoylation site confines b5R to the ER.

The new article reveals that b5R's dual localization relies on a fine balance between N-myristoylation and capture by the signal recognition particle (SRP), which bound to b5R's NH_2-terminal membrane-anchoring region. This binding was weak, however, and was further weakened by myristoylation. The modification caused a conformational change in b5R's NH_2-terminal region that may lower but not eliminate its affinity for SRP. By partly avoiding the ER, b5R is available for insertion into the MOM.

A longer, more hydrophobic anchor, which has a higher affinity for SRP, disrupted MOM targeting and decreased myristoylation. Most of this b5R was found at the ER.

The findings show the importance of weak targeting signals for dual localization. When more of the b5R is needed in the ER, cells could either up-regulate SRP or down-regulate the myristoylation machinery. JCB

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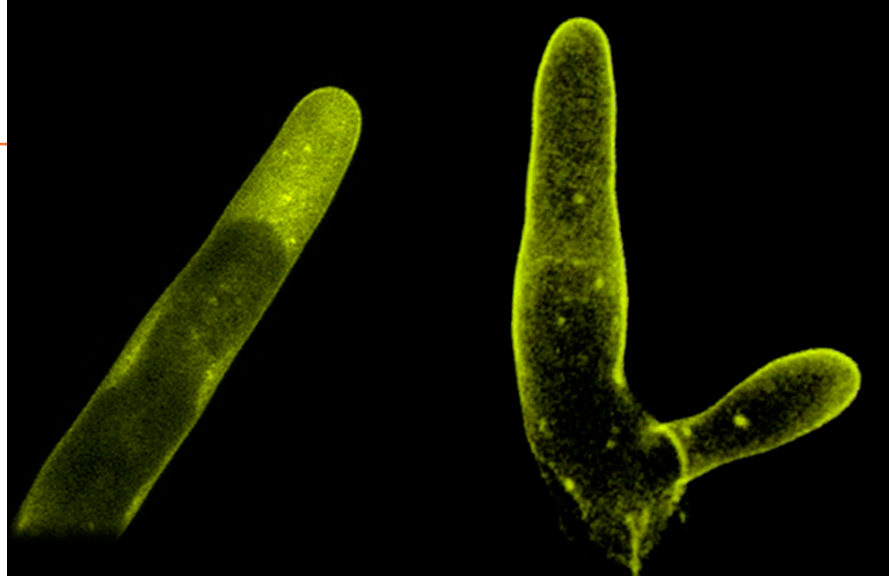
Bringing PIPs to root tips

Tiny hairs on *Arabidopsis thaliana* roots elongate via tip growth, in which new membrane is added specifically at the root hair tip. Vincent et al. (page 801) now show that a phosphatidylinositol transfer protein (PITP) related to yeast Sec14p is critical for this polarized growth, suggesting that PIP_2 may be the start of the polarity cascade in this system.

The authors show that *Arabidopsis* has a large family of these PITPs. One such PITP is AtSfh1p, which, along with its downstream product PIP_2, localized to the tip plasma membrane and on post-Golgi vesicles that accumulate at the hair tips.

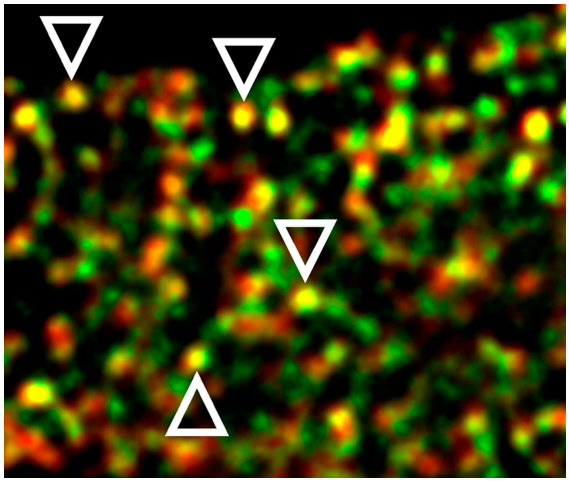


The concentration of PIP_2 (yellow) at the tip (left) of root hairs is lost in the AtSfh1p mutant (right).

AtSfh1p mutation disrupted several aspects of polarity normally found in wild-type hairs and culminated in the loss of tip-directed membrane secretion. These lost polarity cues include the tip localization of PIP_2, a tip-directed F-actin network, strong tip-localized calcium influx, and the microtubule polymerization that normally follows in the wake of high calcium.

In the authors' model, AtSfh1p on post-Golgi vesicles produces PIP_2, which links the vesicles (possibly via interactions with motor proteins) to a tip-directed actin network that can be generated on demand. Once they reach the tip, the vesicles deposit PIP_2 in the plasma membrane and thereby reinforce tip-directed actin polymerization. Vesicles may also carry and deposit calcium channels, thus establishing the calcium signals at the tip. One insult to this system, such as the loss of AtSfh1p, would result in a domino effect that kills root hair polarity.

AtSfh1p and many other *Arabidopsis* PITPs also contain coiled-coil nod domains, which may target the PITPs to distinct subcellular locations. Nitrogen-fixing bacteria express nod domains during nodulation; they might use this trick to subvert AtSfh1p localization and thus polarized membrane secretion while they invade the plant cells. JCB



Active JNK (green) rides with dynein (red) back to the cell body.

Nerve damage surveillance

The regeneration of damaged nerves relies on a JNK-dependent MAPK pathway and the stress-responsive transcription factor it activates, c-Jun. In relatively small epithelial cells, JNK can simply diffuse to the nucleus to turn on c-Jun. But human neurons can be up to a meter long—too long for diffusion to suffice. On page 775, Cavalli et al. suggest that damage communication might be achieved quickly by hooking JNK to axonal vesicles.

JNK interacts with a scaffold protein called Sunday Driver (syd). Syd, in turn, has been proposed to link vesicles to the microtubule motor protein kinesin. With this knowledge in hand, the group now shows that JNK is a surveillance molecule ready to detect and report axonal injuries to the cell body.

JNK and syd were found in murine axons on vesicles that were traveling both out to axon tips (on kinesin motors) and back to the cell body (on dynein). Injuries activated JNK out in axons and enhanced its interaction with the dynein-associated complex dynactin. Axonal injuries are thus expected to bring active JNK to the cell body, where it can turn on c-Jun to start the repair process.

Other molecules in complex with JNK may keep the kinase in its activated form for the long trip, either by protecting JNK's initial phosphorylation or by repeatedly phosphorylating it. As yet, though, it is unclear what other proteins reside in the vesicles. JNK and syd may be simply hitchhiking on vesicles that are transporting synaptic proteins. Alternatively, the vesicles may be dedicated damage repair packages. A cell culture model will be most helpful for the biochemistry that needs to be done next.

Neurons may be an extreme version of a problem that also exists in smaller cells. Although microtubules are not absolutely required for injury responses in epithelial cells, a motor-based transport mechanism may be used normally to improve repair efficiency. JCB